

What is claimed is:

1. An isolated polynucleotide comprising a portion which anneals with high stringency with at least twenty consecutive nucleotide residues of a strand of a human *FEZ1* gene.
2. The isolated polynucleotide of claim 1, wherein the human *FEZ1* gene has the nucleotide sequence SEQ ID NO: 1.
3. The isolated polynucleotide of claim 1, wherein the portion anneals with high stringency with at least thirty consecutive nucleotide residues of at least one strand of the human *FEZ1* gene.
4. The isolated polynucleotide of claim 1, wherein the portion is substantially homologous with at least twenty consecutive nucleotide residues of the human *FEZ1* gene.
5. The isolated polynucleotide of claim 4, wherein the portion is completely homologous with at least twenty consecutive nucleotide residues of at least one strand of the human *FEZ1* gene.
6. The isolated polynucleotide of claim 4, wherein the portion is substantially homologous with at least twenty consecutive nucleotide residues of a *FEZ1* exon region selected from the group consisting of nucleotide residues 112-456, nucleotide residues 1707-2510, and nucleotide residues 4912-5550 of a strand of SEQ ID NO: 1.
7. The isolated polynucleotide of claim 6, wherein the isolated polynucleotide comprises a portion having the nucleotide sequence of a strand of SEQ ID NO: 3.

8. The isolated polynucleotide of claim 6, wherein the isolated polynucleotide further comprises a promoter.
9. The isolated polynucleotide of claim 8, wherein the promoter is a constitutive promoter.
10. The isolated polynucleotide of claim 8, wherein the promoter is an inducible promoter.
11. The isolated polynucleotide of claim 8, wherein the promoter is a tissue-specific promoter.
12. The isolated polynucleotide of claim 1, wherein the isolated polynucleotide is incorporated in a nucleic acid vector.
13. The isolated polynucleotide of claim 1, wherein the isolated polynucleotide is encoded by nucleic acid which is incorporated in a nucleic acid vector.
14. The isolated polynucleotide of claim 1, wherein the isolated polynucleotide has a sequence homologous with a strand of SEQ ID NO: 1.
15. The isolated polynucleotide of claim 1, wherein the isolated polynucleotide is detectably labeled.
16. The isolated polynucleotide of claim 15, wherein the detectably labeled isolated polynucleotide is selected from the group consisting of an immobilized polynucleotide, a polynucleotide linked to a protein of a protein-ligand pair, a polynucleotide linked to a ligand of a protein-ligand pair, a biotinylated polynucleotide,

a polynucleotide linked to a fluorophore, a polynucleotide linked to a chromophore, a polynucleotide linked to an enzyme, and a radio-labeled polynucleotide.

17. The isolated polynucleotide of claim 16, wherein the immobilized polynucleotide is immobilized on the surface of a gene chip.

18. The isolated polynucleotide of claim 1, wherein the isolated polynucleotide is substantially purified.

19. The isolated polynucleotide of claim 1, wherein at least two nucleotide residues of the isolated polynucleotide are linked by a non-naturally occurring linkage other than a phosphodiester linkage.

20. The isolated polynucleotide of claim 19, wherein the non-naturally occurring linkage is selected from the group consisting of phosphonate, phosphorothioate, phosphorodithioate, phosphoramidate methoxyethyl phosphoramidate, formacetal, thioformacetal, diisopropylsilyl, acetamidate, carbamate, dimethylene-sulfide (-CH<sub>2</sub>-S-CH<sub>2</sub>), dimethylene-sulfoxide (-CH<sub>2</sub>-SO-CH<sub>2</sub>), dimethylene-sulfone (-CH<sub>2</sub>-SO<sub>2</sub>-CH<sub>2</sub>), 2'-O-alkyl, and 2'-deoxy-2'-fluoro phosphorothioate, phosphotriester, siloxane, carbonate, carboxymethyl ester, acetamidate, thioether, bridged phosphoramidate, bridged methylene phosphonate, bridged phosphoramidate, bridged phosphorodithioate, bridged methylene phosphonate, phosphorothioate, methylphosphonate, phosphorodithioate, bridged phosphorothioate linkages, bridged sulfone linkages, and combinations of such linkages.

21. The isolated polynucleotide of claim 1, wherein an end of the isolated polynucleotide is nucleolytically blocked.

22. An isolated polynucleotide comprising a portion which has a sequence which anneals with high stringency with at least twenty consecutive nucleotide residues of a strand of SEQ ID NO: 3.

23. A kit for amplifying a portion of a human *FEZ1* gene, the kit comprising a first isolated polynucleotide and a second isolated polynucleotide, wherein the first isolated polynucleotide comprises a portion which anneals with high stringency with at least twenty consecutive nucleotide residues of the coding strand of SEQ ID NO: 1, and wherein the second isolated polynucleotide comprises a portion which anneals with high stringency with at least twenty consecutive nucleotide residues of the non-coding strand of SEQ ID NO: 1.

24. A kit for amplifying a portion of a cDNA generated from a transcript of a human *FEZ1* gene, the kit comprising a first isolated polynucleotide and a second isolated polynucleotide, wherein a portion of the first isolated polynucleotide anneals with high stringency with at least twenty consecutive nucleotide residues of the coding strand of SEQ ID NO: 1, and wherein a portion of the second isolated polynucleotide anneals with high stringency with at least twenty consecutive nucleotide residues of the non-coding strand of SEQ ID NO: 1.

25. An animal cell comprising an exogenous DNA molecule having a portion substantially homologous with at least nucleotide residues 112-456, nucleotide residues 1707-2510, and nucleotide residues 4912-5550 of a strand of SEQ ID NO: 1.

26. The animal cell of claim 25, wherein the exogenous DNA molecule further comprises a promoter operably linked with the portion, whereby the exogenous DNA molecule is expressed in the animal cell.

27. A genetically altered animal comprising a cell into which an exogenous DNA molecule has been artificially introduced, the exogenous DNA

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molecule having a portion substantially homologous with at least the coding region of a strand of a human *FEZ1* gene.

28. The genetically altered animal of claim 27, wherein the exogenous DNA molecule has a portion substantially homologous with at least nucleotide residues 112-456, nucleotide residues 1707-2510, and nucleotide residues 4912-5550 of a strand of SEQ ID NO: 1.

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29. The genetically altered animal of claim 28, wherein the exogenous DNA molecule comprises a portion having a sequence substantially homologous with a strand of SEQ ID NO: 2.

30. An isolated human Fez1 protein.

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31. The isolated human Fez1 protein of claim 30, wherein the protein has an amino acid sequence substantially homologous with SEQ ID NO: 4.

32. The isolated human Fez1 protein of claim 30, wherein the protein has an amino acid sequence completely homologous with SEQ ID NO: 4.

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33. The isolated human Fez1 protein of claim 30, wherein the protein is substantially purified.

34. An isolated antibody which binds specifically with human Fez1 protein.

35. A hybridoma cell which produces antibodies which bind specifically with human Fez1 protein.

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36. A method of determining the cancerous status of a sample tissue, the method comprising comparing *FEZ1* expression in the sample tissue with *FEZ1* expression in a control tissue of the same type, whereby decreased *FEZ1* expression in the sample tissue, relative to *FEZ1* expression in the control tissue, is an indication that the sample tissue is cancerous.

37. The method of claim 36, wherein the sample tissue is a phenotypically abnormal portion of a body tissue of a human, and wherein the control tissue is a phenotypically normal portion of the body tissue.

38. The method of claim 37, wherein the body tissue is an epithelial tissue.

39. The method of claim 37, wherein the body tissue is selected from the group consisting of a gastrointestinal tissue, esophagus tissue, gastric tissue, colon tissue, prostate tissue, breast tissue, a hematopoietic tissue, lung tissue, melanoma tissue, cervical tissue, and ovarian tissue.

40. The method of claim 36, wherein *FEZ1* expression in the sample tissue is compared with *FEZ1* expression in the control tissue by comparing the relative amounts of an indicator in the sample tissue and in the control tissue, wherein the indicator is selected from the group consisting of a *FEZ1* mRNA, a cDNA prepared using a *FEZ1* mRNA, a DNA prepared by amplification of either of these, and Fez1 protein.

41. A method of determining the cancerous status of a sample tissue, the method comprising comparing  
the nucleotide sequence of a *FEZ1*-associated polynucleotide obtained from the sample tissue and  
the nucleotide sequence of a control *FEZ1*-associated polynucleotide,

whereby a difference between the nucleotide sequence of the *FEZ1*-associated polynucleotide obtained from the sample tissue and the nucleotide sequence of the control *FEZ1*-associated polynucleotide is an indication that the sample tissue is cancerous.

42. A method of determining the cancerous status of a human sample tissue, the method comprising comparing the length of an *FEZ1*-transcript-associated polynucleotide obtained from the sample tissue with the length of a control *FEZ1*-transcript-associated polynucleotide, whereby if the length of the *FEZ1*-transcript-associated polynucleotide obtained from the sample tissue is less than the length of the control *FEZ1*-transcript-associated polynucleotide, then this is an indication that the sample tissue is cancerous.

43. A method of determining the cancerous status of a sample tissue, the method comprising assessing *FEZ1* expression in the sample tissue, whereby a substantial absence of *FEZ1* expression in the sample tissue is an indication that the sample tissue is cancerous.

44. The method of claim 43, wherein *FEZ1* expression is assessed by assessing the presence or substantial absence of an indicator selected from the group consisting of a *FEZ1* mRNA, a cDNA prepared using a *FEZ1* mRNA, a DNA prepared by amplification of either of these, and Fez1 protein.

45. A method of determining the cancerous status of a sample tissue, the method comprising detecting abnormal splicing of a *FEZ1* transcript in the sample tissue, whereby abnormal splicing of the *FEZ1* transcript is an indication that the sample tissue is cancerous.

46. The method of claim 45, wherein abnormal splicing of the *FEZ1* transcript is detected by assessing the ability of an exon boundary polynucleotide probe

to anneal with a *FEZ1*-transcript-associated polynucleotide with high stringency, wherein the exon boundary polynucleotide probe is capable of annealing with high stringency with terminal portions of two sequential *FEZ1* exons when the terminal portions are adjacent, but not when the terminal portions are not adjacent.

47. A method of modulating abnormal proliferation of a human cell having an altered *FEZ1* gene, the method comprising providing an exogenous source of Fez1 protein to the cell, whereby abnormal proliferation of the cell is inhibited, delayed, or prevented.

48. The method of claim 47, wherein the exogenous source of Fez1 protein is a composition comprising an isolated human Fez1 protein.

49. The method of claim 48, wherein the human Fez1 protein has the amino acid sequence SEQ ID NO: 4.

50. The method of claim 47, wherein the exogenous source of Fez1 protein comprises an expression vector comprising a polynucleotide having a coding region which encodes a functional Fez1 protein, whereby the polynucleotide is expressed in the cell.

51. The method of claim 50, wherein the polynucleotide comprises a human *FEZ1* gene.

52. The method of claim 50, wherein the coding region comprises a portion having the nucleotide sequence of a strand of SEQ ID NO: 3.

53. The method of claim 47, wherein the polynucleotide further comprises a constitutive promoter operably linked with the coding region.



54. The method of claim 47, wherein the polynucleotide further comprises an inducible promoter operably linked with the coding region, the method further comprising administering an inducer of the inducible promoter to the cell.

55. The method of claim 47, wherein the polynucleotide further comprises a tissue-specific promoter operably linked with the coding region.

56. The method of claim 47, wherein the polynucleotide further comprises a wild-type *FEZ1* promoter region.

57. A method of inhibiting tumorigenesis in a human cell, the method comprising providing to the cell an expression vector comprising a polynucleotide having a coding region which encodes a functional Fez1 protein, whereby tumorigenesis is inhibited in the cell.

58. A method of reversibly inducing proliferation of a cell, the method comprising providing an inhibitor of *FEZ1* expression to the interior of the cell, whereby proliferation of the cell is induced.

59. The method of claim 58, wherein the inhibitor is an isolated polynucleotide comprising a portion which anneals with high stringency with at least twenty consecutive nucleotide residues of a strand of a human *FEZ1* gene.

60. The method of claim 59, wherein the isolated polynucleotide is delivered to the interior of the cell by administering a gene vector comprising a promoter operably linked with the isolated polynucleotide to the cell.

61. The method of claim 58, wherein the cell is located in the body of an animal.

62. The method of claim 61, wherein the animal is a human.

63. A method of determining whether a test compound is an inducer of cell proliferation, the method comprising incubating a cell which comprises a functional *FEZ1* gene in the presence of the test compound and assessing expression of *FEZ1* in the cell, whereby if expression of *FEZ1* in the cell is decreased, relative to expression of *FEZ1* in a cell of the same type incubated in the absence of the test compound, then the test compound is an inducer of cell proliferation.

64. A method of determining whether a test compound is effective to retard abnormal proliferation of a cell having an altered *FEZ1* gene, the method comprising incubating the cell in the presence of the test compound and assessing expression of *FEZ1* in the cell, whereby if expression of *FEZ1* in the cell is increased, relative to expression of *FEZ1* in a cell of the same type incubated in the absence of the test compound, then the test compound is effective to retard abnormal proliferation of a cell.

65. A method of determining whether Fez1 protein binds with polynucleotides having a test nucleotide sequence, the method comprising contacting Fez1 protein and a test polynucleotide having the test nucleotide sequence, wherein at least one of the Fez1 protein and the test polynucleotide is detectably labeled, and thereafter assessing whether a detectably labeled Fez1-polynucleotide complex is formed, whereby formation of the complex is an indication that Fez1 protein binds with polynucleotides having the test nucleotide sequence.

66. A method of identifying an inducer of cell proliferation, the method comprising

contacting Fez1 protein and a polynucleotide with which Fez1 protein binds in the presence and absence of a test compound, and

assessing formation of a Fez1-polynucleotide complex, whereby decreased formation of the complex in the presence of the test compound, relative to formation of Fez1-polynucleotide complex in the absence of the test compound is an indication that the test compound is an inducer of cell proliferation.

67. A kit for selecting an anti-cancer therapeutic compound for administration to a human afflicted with a cancer, the kit comprising a plurality of candidate anti-cancer therapeutic compounds and a reagent for assessing expression of *FEZ1* in a cell.

68. A method of inducing a cell to proliferate, the method comprising inhibiting expression of *FEZ1* in the cell, whereby the cell is induced to proliferate.

69. The method of claim 68, wherein the cell is removed from a human.

70. The method of claim 69, wherein the cell is returned to the human after inhibiting expression of *FEZ1* in the cell.

71. The method of claim 68, wherein the cell is present in the body of a human.

72. The method of claim 68, wherein expression of *FEZ1* in the cell is inhibited by providing to the interior of the cell an isolated polynucleotide comprising a portion which anneals with high stringency with at least twenty consecutive nucleotide residues of a strand of a human *FEZ1* gene.

73. An enhanced human cell culture technique, the technique comprising incubating human cells according to a known human cell culture technique and inhibiting *FEZ1* expression in the cells.

74. A method of detecting *FEZ1* expression in a sample tissue, the method comprising  
labeling an isolated antibody which binds specifically with human Fez1 protein and contacting a preparation of the isolated antibody with the sample tissue,  
thereafter rinsing the tissue sample, whereby non-specifically bound antibodies are rinsed from the tissue sample, and  
assessing the presence of labeled antibodies in the tissue sample, whereby the presence of labeled antibodies in the tissue sample is an indication that *FEZ1* is expressed in the tissue sample.

75. A method of determining whether a test compound is useful for alleviating a disorder associated with aberrant tubulin polymerization, the method comprising comparing  
tubulin polymerization in a first assay mixture which comprises tubulin, Fez1, and the test compound and  
tubulin polymerization in a second assay mixture which comprises tubulin and Fez1, but which does not comprise the test compound,  
wherein a difference between tubulin polymerization in the first and second assay mixtures is an indication that the test compound is useful for alleviating the disorder.

76. The method of claim 75, wherein the disorder is a tubulin hyperpolymerization disorder.

77. The method of claim 75, wherein the disorder is a tubulin hypopolymerization disorder.

78. The method of claim 75, wherein the disorder is selected from the group consisting of a disorder associated with aberrant initiation of mitosis, a disorder associated with aberrant modulation of the rate and stage of mitosis, a disorder associated with aberrant modulation of the initiation and rate of cell proliferation, a disorder associated with aberrant modulation of the initiation and rate of cell growth, a disorder associated with aberrant modulation of cell shape, a disorder associated with aberrant modulation of cell rigidity, a disorder associated with aberrant modulation of cell motility, a disorder associated with aberrant modulation of the rate of cellular DNA replication, a disorder associated with aberrant modulation of the stage of cellular DNA replication, a disorder associated with aberrant modulation of the intracellular distribution of organelles, a disorder associated with aberrant modulating the metastatic potential of a cell, and a disorder associated with aberrant modulation of cellular transformation from a non-cancerous to a cancerous phenotype.

79. The method of claim 75, wherein the disorder is selected from the group consisting of tumorigenesis, tumor survival, tumor growth, and tumor metastasis.

80. The method of claim 75, wherein the difference is a difference between the rate of tubulin polymerization in the first and second assay mixtures.

81. The method of claim 75, wherein the difference is a difference between the extent of tubulin polymerization in the first and second assay mixtures.

82. The method of claim 75, wherein the test compound is selected from the group consisting of a fragment of Fez1, a peptidomimetic of a fragment of Fez1, a fragment of tubulin, a peptidomimetic of a fragment of tubulin, a fragment of EF1- $\gamma$ , and a peptidomimetic of a fragment of EF1- $\gamma$ .

83. The method of claim 75, wherein the first and second assay mixtures are substantially identical, but for the presence or absence of the test compound.

84. A method of determining whether a test compound is useful for alleviating a disorder associated with aberrant phosphorylation of Fez1, the method comprising comparing

phosphorylation of Fez1 in a first assay mixture which comprises Fez1, at least one kinase, a phosphate source, and the test compound and

phosphorylation of Fez1 in a second assay mixture which comprises Fez1, the kinase, and the phosphate source, but which does not comprise the test compound, wherein a difference between phosphorylation of Fez1 in the first and second assay mixtures is an indication that the test compound is useful for alleviating the disorder.

85. The method of claim 84, wherein the disorder is selected from the group consisting of tumorigenesis, tumor survival, tumor growth, and tumor metastasis.

86. A method of determining whether a test compound is useful for alleviating a disorder associated with aberrant phosphorylation of Fez1, the method comprising comparing

phosphorylation of Fez1 in a first assay mixture which comprises phosphorylated Fez1, at least one phosphatase, and the test compound and

phosphorylation of Fez1 in a second assay mixture which comprises phosphorylated Fez1 and the phosphatase, but which does not comprise the test compound,

wherein a difference between phosphorylation of Fez1 in the first and second assay mixtures is an indication that the test compound is useful for alleviating the disorder.

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93. A method of inhibiting tumorigenesis in a human, the method comprising administering to the human a compound selected from the group consisting of an inducer of *FEZ1* gene expression, an enhancer of *FEZ1* gene expression, a inhibitor of Fez1 phosphorylation, an enhancer of phosphorylated-Fez1 dephosphorylation, an agent that inhibits binding of Fez1 with EF1- $\gamma$ , and an agent that inhibits binding of Fez1 with tubulin.

94. An isolated polynucleotide comprising a portion which is substantially homologous with at least 20 consecutive nucleotide residues of a strand of a human *FEZ1* gene.

95. The isolated polynucleotide of claim 94, wherein the human *FEZ1* gene has the nucleotide sequence SEQ ID NO: 1.

96. The isolated polynucleotide of claim 94, wherein the portion is at least 90% homologous with at least 20 consecutive nucleotide residues of a strand of a human *FEZ1* gene.

97. The isolated polynucleotide of claim 94, wherein the portion is substantially with at least 50 consecutive nucleotide residues of a strand of a human *FEZ1* gene.

98. The isolated human Fez1 protein of claim 30, wherein the protein has an amino acid sequence which is substantially homologous with SEQ ID NO: 4.

99. An isolated polypeptide which has an amino acid sequence which is substantially homologous with at least 20 consecutive residues of SEQ ID NO: 4.

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